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10/563,195	04/03/2006	Alison Velyian Todd	J&J5215USPCT	6479
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Sullivan & Worcester LLP 1666 K Street, N.W. Washington, DC 20006				
EXAMINER				
BHAT, NARAYAN KAMESHWAR				
ART UNIT		PAPER NUMBER		
1634				
NOTIFICATION DATE		DELIVERY MODE		
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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**Advisory Action
Before the Filing of an Appeal Brief**

Application No.

10/563,195

Applicant(s)

TODD ET AL.

Examiner

NARAYAN K. BHAT

Art Unit

1634

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 18 June 2009 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
(a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
(b) ☐ They raise the issue of new matter (see NOTE below);
(c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
(d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
The status of the claim(s) is (or will be) as follows:
Claim(s) allowed: None.
Claim(s) objected to: None.
Claim(s) rejected: 1-37.
Claim(s) withdrawn from consideration: 38.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:
See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____.
13. ☐ Other: _____.

/JD Schultz/
Supervisory Patent Examiner, Art Unit 1635

Continuation of 11- does NOT place the application in condition for allowance because claims 1-4, 14-31, 33 and 35-37 have been rejected as being unpatentable over Gitan et al in view of Bransteitter et al. Claims 1 and 4-13 have been rejected as being unpatentable over Gitan et al, Bransteitter et al and Kuhn et al. Claims 1 and 32 have been rejected as being unpatentable over Gitan et al, Bransteitter et al and Opdecamp et al. Claims 1 and 34 have been rejected as being unpatentable over Gitan et al, Bransteitter et al and Paulson et al. Applicant's arguments filed on June 18, 2009 with respect to teachings of cited references are not persuasive for the reasons as described below.

Spelling Correction:

Amendments to claims 5, 8, 10-15, 26, 29 and 31 to correct spelling of certain words conforming to English language practice in the USA have been reviewed and entered.

Sequence listing:

Sequence listing filed on June 18, 2009 for correcting the errors noted by the office has been reviewed and accepted by the office.

Claim rejections 35 USC103 (a):

Rejections being unpatentable over Gitan et al in view of Bransteitter et al:

Applicants argue that there is no disclosure in Gitan et al of the use of an enzyme which differentially modifies methylated cytosine and Unmethylated cytosine in single stranded DNA and that deficiency is not cured by Bransteitter et al (Remarks, pg. 8, paragraphs 4 and 5). This argument is not persuasive because Applicants have asserted that Gitan et al teaches the recited steps 'a' to 'd' of independent claim 1 except for the use of an enzyme which differentially modifies methylated cytosine and unmethylated cytosine in single stranded DNA (Remarks, pg. 8, paragraph 4). Applicants have also asserted that Bransteitter et al teach an enzyme treatment to differentially modulate single stranded DNA comprising methylated and unmethylated cytosine (Remarks, pg. 8, paragraph 5). Furthermore, courts have ruled that Applicant's arguments by attacking references individually are not persuasive wherein the rejections are based on combinations of references (See In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986)). In the instant case, as described in the final office action, Gitan et al in view of Bransteitter et al teaches recited steps 'a' to 'd' as claimed and therefore arguments are not persuasive. Also, Applicants have not provided support documents or affidavits or reasons why the enzyme reaction of single stranded DNA of Bransteitter et al would not work in place of bisulfite reaction of Gitan et al. For these reasons Applicants arguments are not persuasive.

Applicants further argue that Bransteitter et al do not disclose measuring the presence of or level of alkylated cytosine in a DNA sample (Remarks, pg. 8, paragraph 5, lines 3 and 4). This argument is not persuasive because claim merely requires an active step of determining the level of enzymatic modification of the target region by the enzyme, which is taught by Bransteitter et al (Fig. 4a). Furthermore, claim as recited measuring the level of alkylated cytosine in a DNA sample is not an active step. Nonetheless, Gitan et al teaches the level of alkylated cytosine in a DNA sample (Fig. 3). Furthermore, a preamble is generally not accorded any patentable weight where it merely recites the purpose of a process and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps are able to stand alone. See In re Hirao, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and Kropp v. Robie, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951). For these reasons, arguments are not persuasive.

Applicants further argue that one of skill in the art would not combine Gitan et al and Bransteitter et al and have a reasonable expectation of successfully practicing the claimed invention (Remarks, pg. 8, paragraph 5, lines 5 and 6). This argument is not persuasive because as described above, Applicants have not provided support documents or affidavits or reasons why the enzyme reaction of single stranded DNA of Bransteitter et al would not work in place of bisulfite reaction of Gitan et al. Furthermore, arguments of counsel are not found persuasive in the absence of factual showing. MPEP 716.01(c) makes clear that "The arguments of counsel cannot take the place of evidence in the record. In re Schulte, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long-felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant. As described above, Gitan et al in view of Bransteitter et al teach recited steps 'a' to 'd' as claimed and therefore arguments are not persuasive.

Applicants further argue that the office action fails to meet its burden in making prima facie conclusion of obviousness (Remarks, pg. 8, paragraph 5, lines 6 and 7). This argument is not persuasive because as described in the final office action, both Gitan et al and Bransteitter et al teaches the method steps for detecting the methylation and therefore method steps are combinable. As described above, Gitan et al teaches bisulfite treatment for long hours to differentially modulate single stranded DNA comprising unmethylated and methylated cytosine, where as Bransteitter et al teaches an enzyme treatment for minutes for differentially modulating single stranded DNA comprising unmethylated and methylated cytosine for expediting the detection of methylation pattern in the method of Gitan et al. One having the skill in the art would like to use an enzyme for detecting methylation status in a target genome, because it requires less time and does not require additional steps of purifying target as also taught by Bransteitter et al. Since Bransteitter et al provides the teachings, suggestions and motivation for using enzyme for modifying the alkylated cytosine in the method of Gitan et al, arguments are not persuasive.

Applicants further argue that understanding the importance of methylation pattern in biological processing do not suffice as

articulated reasoning (Remarks, pg. 9, paragraph 1). This argument is not persuasive because as described above, Bransteitter et al provides the teachings, suggestions and motivation for using enzyme for modifying the alkylated cytosine in the method of Gitan et al and therefore arguments are not persuasive.

Rejections being unpatentable over Gitan et al, Bransteitter et al and Kuhn et al:

Applicant's arguments regarding the teachings of Kuhn et al are directed towards not curing the deficiency of Gitan et al and Bransteitter et al (Remarks, pg. 9, paragraph 3). This argument is not persuasive because as described above, Gitan et al and Bransteitter et al teach recited steps 'a' to 'd' as claimed and therefore arguments are not persuasive.

Rejections being unpatentable over Gitan et al, Bransteitter et al and Opdecamp et al:

Applicant's arguments regarding the teachings of Opdecamp et al are directed towards not curing the deficiency of Gitan et al and Bransteitter et al (Remarks, pg. 9, paragraph 5). This argument is not persuasive because as described above, Gitan et al and Bransteitter et al teach recited steps 'a' to 'd' as claimed and therefore arguments are not persuasive.

Rejections being unpatentable over Gitan et al, Bransteitter et al and Paulson et al:

Applicant's arguments regarding the teachings of Paulson et al are directed towards not curing the deficiency of Gitan et al and Bransteitter et al (Remarks, pg. 10, paragraph 3). This argument is not persuasive because as described above, Gitan et al and Bransteitter et al teach recited steps 'a' to 'd' as claimed and therefore arguments are not persuasive.